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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,540	03/16/2004	Blake Pepinsky	BII-008.02	4023

25181 7590 05/25/2007

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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
05/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,540	PEPINSKY ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/27/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-62* is/are pending in the application.

4a) Of the above claim(s) *61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-60 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :11/10/06; 10/19/06; 04/25/05; 07/22/04.

Detailed Office Action

Election/Restrictions:

1a. Applicants' election with traverse of Group 15, (claims 41-60), filed on 27 February 2007 is acknowledged.

Applicants' ground of traversal is that it would not pose an undue burden to examine and search the inventions of the elected Group 15 and Group 75, (claim 62) a method of preparing said polypeptide.

This traversal is found persuasive, therefore, Groups 15 and 75 are rejoined and will be searched and examined together.

The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Claims:

1b. Claims 41-62 are pending, of which claims 41-60, 62 and SEQ ID NO:41 will be searched and examined.

Claim 61, is withdrawn from consideration by the Examiner as it is drawn to non-elected invention.

Information Disclosure Statement:

2. The information disclosure statements (IDS) submitted on 11 November 2006, 19 October 2006, 25 April 2005 and 22 July 2004 have been received and comply with the provisions of 37 CFR §1.97 and §1.98. The references have been placed in the application file and the information referred to therein has been considered as to the merits. References cited on the IDS of 22 July 2004 have been considered in the parent Application 09/832,658.

Claim Objections:

3. Claims 41, 43, 45, 49, 53, 59, 60 and 62 are objected to because of the following informalities: Claims 41, 43, 45, 49, 53, 59, 60 and 62 recite non-elected sequences. Appropriate correction is required. It is acknowledged that the preliminary amendment filed on 18 August 2006, relate to SEQ ID NOs:27-56, not SEQ ID NOs:25-56.

Priority:

4. Based on the information given by Applicants and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in this application is entitled to the effective filing date of 16 October 1998, which is the filing date of the Provisional parent application 60/104,572.

Claim rejections- Obviousness-type Double patenting:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 41-60 and 62 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,962,978. Although the conflicting claims are not identical, they are not patentably distinct from each other because: in summary, the instant claims 41-60 are drawn to a physiologically active composition, comprising a glycosylated interferon beta 1a comprising the amino acid sequence set forth in SEQ ID NO:41, coupled to a non-naturally occurring polymer at an N-terminal end or C-terminal, wherein said composition is stable and soluble in aqueous solutions, wherein the polymer molecule weight is from about 5 to 40 kilodaltons, wherein said composition retains equal or at least 2 fold greater activity relative to the unmodified interferon beta-1a, wherein said interferon beta 1a is a fusion protein. Claims 1-24 of U.S. Patent No. 6,962,978 (having the same inventive entity as the instant application), are drawn to a physiologically active composition, comprising a glycosylated interferon beta 1a comprising the amino acid sequence set forth in SEQ ID NO:25 or 26, coupled to non-naturally occurring polymer at an N-terminal end or at a C-terminal end wherein said composition retains equal or at least 2 fold greater activity relative to the unmodified interferon beta-1a,

wherein said interferon beta 1a is a fusion protein, wherein said composition is stable and soluble in aqueous solutions. However, the claimed invention and the patented invention, although they comprise different amino acid sequences are obvious over each other. The claimed invention is obvious over the patented invention, because one of ordinary skill in the art, would be able to follow the disclosure in patent 6,962,978, and conjugate the interferon beta 1a of SEQ ID NO:41, with great expectation of success that the resulting product would have an increased half-life and retain the desired activity. Therefore, allowance of the pending claims, would have the effect of extending the enforceable life of the allowed claims beyond statutory limit.

Claim Rejections - 35 U.S.C. § 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 41, 43, 58, 59, 60, 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claims 41,43, 58, 59, 60, 62 recite ".....any one of SEQ ID NO:", however, since Applicants elected SEQ ID NO:41 to be searched and examined, the claims should be amended to delete any reference to more than one SEQ ID NO:. Appropriate correction is required. Claims 42-44 are rejected under 35 U.S.C. 112, second paragraph, in so far as they depend from claim 41 for the limitations set forth above.

Claim rejections-35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7a. Claims 41-42, 45-46, 49-50, 53-59 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mark et al (WO8302461, issued on 21 July 1983) in view of Katre et al (US Patent 4,766,106, issued 23 August 1988, cited on the IDS filed on 25 April 2005).

The instant claims are drawn to a physiologically active composition, comprising a glycosylated interferon beta 1a comprising the amino acid sequence set forth in SEQ ID NO:41, coupled to a non-naturally occurring polymer at an N-terminal end or C-terminal end, wherein said composition is stable and soluble in aqueous solutions, wherein the polymer molecule's weight is from about 5 to 40 kilodaltons, wherein said composition retains equal or at least 2 fold greater activity relative to the unmodified interferon beta-1a and a method of preparing said composition.

Mark et al disclose an isolated interferon beta-1 that shares 100% homology to the interferon beta-1 of SEQ ID NO:41 recited in the instant claims and shows that said interferon beta-1 exhibits antiviral activity , (see attached sequence query Appendix A and table V of WO8302461).

However, Mark et al do not teach their interferon beta-1 conjugated to a non-naturally occurring polymer, at an N-terminal end or C-terminal end, wherein said composition is stable and soluble in aqueous solutions, wherein the polymer molecule weight is from about 5 to 40 kilodaltons, wherein said composition retains equal or at least 2 fold greater activity relative to the unmodified interferon beta-1b and a method of preparing said composition.

Katre et al disclose a biologically active interferon-beta, conjugated to a polyethylene glycol polymer, wherein said IFN-beta can by glycosylated, wherein the polymer molecule weight is from about 350 to 40,000 Daltons and a method of preparing said conjugated IFN-beta (see abstract, column 3, lines 65-68, column 6, lines 45-68, column 9, lines 5-12). The 1FN-β disclosed by Kate et al is conjugated to polyethylene glycol via an amide linkage, is conjugated via the N-terminal and has higher antiviral activity than the unmodified 1FN- beta, (see column 8, line 30, columns 9 and 10, Example VII and table III on page 24). The IFN- beta disclosed by Katre et al has a substitution at position 17, wherein a cysteine is replaced with a serine.

Therefore, It would have been prima facie obvious at the time of the instant invention, for one skilled in the art to modify the IFN- beta-1 taught by Mark et al, by following the procedure for pegylating interferon beta taught by Katre et al, because

Katre et al taught that modifying IFN- beta by pegylating it renders it more soluble, while retaining the desired activity and also increases the in vivo half life, (see top of column 4). One of ordinary skill in the art would have been motivated to combine the teachings of Mark et al and Katre et al, because it was known at the time of filing that IFN-beta was useful as an antiviral drug and improving its solubility and increasing its in vivo half-live would have been a highly advantageous endeavor.

7b. Claims 43, 44, 47, 48 and 51, 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mark et al in view of Katre et al, (see above) further in view of Capon et al (U.S. Patent 5,116,964, issued on 26 May 1992).

Claims 43, 44, 47, 48 and 51, 52 further limit the claimed invention, wherein the claimed composition is a fusion protein fused to a portion of an imunoglobulin molecule.

The teachings of Mark et al and Katre et al have been set forth above in section 6a of this office action, however, neither Mark et al nor Katre et al teach a composition comprising a fusion of a biologically active interferon-beta, conjugated to a polyethylene glycol polymer.

Capon et al teach chimeric polypeptides comprising ligand binding partners fused to stable plasma proteins which is capable of extending the in vivo plasma half-life of the ligand binding partner, (see abstract and column 5, lines 14-20).

At column 4, lines 38-43, Capon states that the immunoglobulin (Ig) fusions of the invention "serve to prolong the in vivo plasma half-life of the ligand binding partner..." and "facilitate its purification by protein A". Also taught are recombinant materials for making such a fusion protein, vectors and expression; see columns 15-16. Preferred

embodiments include sequences including the hinge regions of IgG-1, -2, -3 or -4, IgA, IgE, IgD and IgM, see column 14, lines 40-45 (the first domain of the constant region can be omitted). The preferred species of Ig was human, see claims 8-9. Capon states that the DNA sequences for the Ig chains were well known in the art at the time the invention was made, see column 15 beginning at line 40.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the pegylated interferon-beta taught by Mark et al, which is pegylated by following the disclosure of Katre et al, to make fusion of the pegylated interferon-beta as taught by Capon et al. The person of ordinary skill in the art would have been motivated to make the modification in view of Capon's disclosure that fusion proteins facilitate purification of desired proteins and to further increase the in vivo half-life of the peyglated interferon -beta. Accordingly, the invention, taken as a whole, is prima facie obvious over the cited prior art.

Conclusion

8. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0853. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
04 May 2007

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER

Appendix A

<!--StartFragment-->RESULT 1
AAP30219
ID AAP30219 standard; protein; 166 AA.
XX
AC AAP30219;
XX
DT 25-MAR-2003 (revised)
DT 25-MAY-1992 (first entry)
XX
DE Sequence of interferon (HuIFN) -beta-1 encoded by plasmid pDM101/trp/beta
DE -1.
XX
KW Hybrid interferon; antiviral; therapy; cancer; tumour.
XX
OS Homo sapiens.
XX
PN WO8302461-A.
XX
PD 21-JUL-1983.
XX
PF 19-JAN-1982; 82US-00340782.
XX
PR 19-JAN-1982; 82US-00340782.
PR 03-FEB-1983; 83US-00463574.
PR 15-JUL-1985; 85US-00755265.
XX
PA (CETU) CETUS CORP.
PA (CETU) CETUS CORP.
XX
PI Mark DF, Creasey AA;
XX
DR WPI; 1983-723186/30.
DR N-PSDB; AAN30152.
XX
PT Multi:class hybrid interferon poly:peptide(s) - with restricted antiviral
PT and cell growth regulatory activities.
XX
PS Example; Fig 5; 61pp; English.
XX
CC The inventors claim a multiclass hybrid interferon polypeptide and a DNA
CC unit having a nucleotide sequence which encodes it. Pref. the AA sequence
CC consists of alpha and beta interferons. Pref. IF1 is (i) the 1-73 AA seq.
CC of HuIFN-alpha-1 (and IF2 is the 74-166 AA seq. of HuIFN-beta-1) (see
CC AAN30155, AAP30222); or (ii) the 1-41 AA seq. of HuIFN-alpha-61A (and IF2
CC is the 43-166 AA seq. of HuIFN-beta-1) (see AAN30160, AAP30227).
CC Alternativeley IF1 is the amino terminal end of a beta-IF and IF2 is the
CC carboxy terminal of an alpha-IF (esp. the 1-73 seq. of HuIFN-beta-1 and
CC the 74-167 seq. of HuIFN-alpha-1 resp.) (see AAN30156, AAP30223). In the
CC examples plasmids pGW5 and pDM101/trp/beta-1 and p-alpha-61A were used
CC (see AAN30151, AAN30152, AAN30157). HinfI was used to digest the DNA
CC sequences in the region of significant handicaps (see AAN30153, AAN30154,
CC AAN30158, AAN30159), and the restriction fragments were ligated to form
CC hybrid DNA. (Updated on 25-MAR-2003 to correct PA field.)
XX
SQ Sequence 166 AA;

  Query Match   100.0%; Score 874; DB 1; Length 166;
  Best Local Similarity   100.0%; Pred. No. 2.4e-69;
  Matches 166; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIY 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1 MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIY 60

```
Qy          61 EMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSL 120
               ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          61 EMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSL 120

Qy         121 HLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN 166
               ||||||||||||||||||||||||||||||||||||||||||||||
Db         121 HLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN 166

<!--EndFragment-->
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